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PATENT  
Attorney Docket No. ISIS-10468

**IN THE SPECIFICATION:**

Please replace the paragraphs beginning on page 9, line <sup>9</sup> 30 and ending on line 15 with the following amended paragraphs:

Figure 20A indicates predicted and actual mass data with scoring parameters for length heteroplasmy (HVR1-1-outer-variants 1 and 2) in the digest segment from position 94 to 145(variant 1) (SEQ ID NO:44)/146(variant 2) (SEQ ID NO:45) are shown.

Figure 20B indicates that, whereas sequencing fails to resolve the variants due to the length heteroplasmy, mass determination detects multiple species simultaneously and also indicates abundance ratios. In this case, the ratio of variant 1 (SEQ ID NO:46, top sequence) to variant 2 (SEQ ID NO:47) (short to long alleles) is 1:3.

Please amend the paragraph on page 25, lines 8-25, as follows:

-- In another embodiment of the present invention, the methods disclosed herein for mtDNA analysis can be used to identify the presence of heteroplasmic variants and to determine their relative abundances. As used herein, "mitochondrial diseases" are defined as diseases arising from defects in mitochondrial function which often arise as a result of mutations and heteroplasmy. If the defect is in the mitochondrial rather than the nuclear genome unusual patterns of inheritance can be observed. This embodiment can be used to determine rates of naturally occurring mutations contributing to heteroplasmy and to predict the onset of mitochondrial diseases arising from heteroplasmy. Examples of mitochondrial diseases include, but are not limited to: Alpers Disease, Barth syndrome, Beta-oxidation Defects, Carnitine-Acyl-Carnitine Deficiency, Carnitine Deficiency , Co-Enzyme Q10 Deficiency, Complex I Deficiency, Complex II Deficiency, Complex III Deficiency , Complex IV Deficiency, Complex V Deficiency, COX Deficiency, CPEO, CPT I Deficiency, CPT II Deficiency, Glutaric Aciduria Type II, KSS, Lactic Acidosis, LCAD, LCHAD, Leigh Disease or Syndrome, LHON, Lethal Infantile Cardiomyopathy, Luft Disease, MAD, MCA, MELAS, MERRF, Mitochondrial Cytopathy, Mitochondrial DNA Depletion, Mitochondrial Encephalopathy, Mitochondrial Myopathy, MNGIE, NARP, Pearson Syndrome, Pyruvate Carboxylase Deficiency, Pyruvate